UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION	**MDL No. 2875** **HON. ROBERT B. KUGLER** **CIVIL NO. 19-2875 (RBK)**
THIS DOCUMENT RELATES TO ALL CASES	

PLAINTIFFS' BRIEF IN OPPOSITION TO ZHP DEFENDANTS' MOTIONS IN LIMINE

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1. **ZHP's motion regarding internal communications on regulatory issues.**

ZHP's motion focuses on two instances in which Prinston's head of quality, Remonda Gergis, criticized ZHP's lack of cGMP compliance. ZHP's inadequate overall approach to quality and the fact that Prinston was on notice of ZHP's inadequate overall approach to quality are relevant facts. There is nothing unduly prejudicial in showing the jury that these issues were recognized years before ZHP's cGMP failures with the valsartan products. If the Court has any concerns, at the least this information should be permitted if ZHP makes (and is permitted to make) any statements about its quality record or adherence to cGMPs in general.

2. **ZHP's motion regarding destruction of inadequately tested batches of valsartan API.**

ZHP paints its August 2017 destruction of an out of specification ("OOS") batch—meaning it failed to meet specifications—of valsartan as a routine non-event. ZHP emphasizes that this "was almost a year before ZHP first learned that its valsartan API contained NDMA. . . As a result, there is no evidence that ZHP had a duty to retain these OOS samples of valsartan API in August 2017, and certainly no reason to suggest that ZHP acted improperly in discarding valsartan batches C5191-17-023/024." (ZHP Br. 4).

However, that logic is built on a false foundation since this deviation investigation began on August 2, 2017—after Jinsheng Lin sent his July 27, 2017 email confirming that there was NDMA in the valsartan and identified the root cause. That email was sent to Jucai Ge, the head of quality assurance, Linda Lin, the head of regulatory, Min Li, the head of CEMAT where Mr. Lin worked, and Peng Dong, the head of the technical department, among others. ZHP's explanation is not credible or faithful to the facts, and certainly is not a reason to withhold this document from the jury.

The crux of the issue is that ZHP inadequately evaluated the OOS finding in a commercial batch of valsartan API beginning on August 2, 2017. ZHP never identified the impurity due to inadequate testing, and **did not identify the root cause, even though ZHP was required by the controlling SOP,** [redacted] Then ZHP inexplicably destroyed this OOS batch on August 22, 2017. (Jucai Ge 4/28/21 Dep. Tr., 164:13-24, 165:16-166:11, 174:6-175:6, 176;11-14, 180:21-182:5, 182:16-183:4 (Ex. 37)).[1] This is a highly relevant snapshot of ZHP's inadequate approach to quality overall, and the context within which ZHP failed to prevent the

[1] Unless otherwise noted, the exhibits cited in this brief are attached to Adam M. Slater's certification in opposition to Defendants' motions in limine.

contamination of the valsartan API.

Also unstated in ZHP's motion is that the FDA cited the destruction of this API batch in the Establishment Inspection Report against ZHP ("EIR"):

> OBSERVATION 3
>
> **The system for managing quality to ensure confidence that the API will meet its intended specifications for quality and purity is not adequate in that your quality unit lacks written procedures and the authority and responsibility to ensure all critical deviations are thoroughly investigated.**
>
> Specifically,
>
> * * *
>
> b) major Deviation DDW02-17003 was initiated August 2, 2017 and closed September 11, 2017 for Valsartan batches D5191-17-023 and D5191-17-024 with OOS results for a single unknown impurity (specification < 0.10%). You confirmed OOS results for Valsartan batches D5191-17-023 single unknown impurity 0.33%, and DS191-17-024 single unknown impurity 0.38%.
>
> i) **you did not identify a root cause for the single unknown impurity results in batches D5191-17-023 and DS191-17-024**. You stated the root cause was probably due to occasional fluctuation in your manufacturing process. **You did not attempt to identify this single unknown impurity. You did not attempt to identify the source of fluctuations in your manufacturing process for Valsartan.**
>
> ii) **you did not develop an adequate Corrective Action and Preventive Action (CAPA) plan.** ….
>
> iii) **you did not conduct a thorough risk assessment.** ….
>
> * * *
>
> Supporting Evidence and Relevance
>
> * * *
>
> I asked Mr. Dong if the firm attempted to identify the single unknown impurity. Mr. Dong stated no. I asked Mr. Jinyi Li, QA Manager West Zone, if the firm identified the single unknown impurity. Mr. J. Li

> stated no. Mr. J. Li further stated historically it is a small peak so the firm thinks it is an isolated case. **Dr. Li stated it is not necessary to identify a single unknown impurity at this level.**
>
> * * *
>
> **Deviation DDW02-17003 did not include investigation of the raw material used in the manufacture of Valsartan to review the quality of the raw materials or identify any OOT raw material test results.**
>
> * * *
>
> **I asked Mr. Dong if the firm attempted to identify the source of fluctuation in the firm's manufacturing process for Valsartan. Mr. Dong stated no,** the firm reviewed the batch record and did not identify any abnormalities. The firm identified a set of possible factors that may impact the size of the single unknown impurity. I asked Mr. Dong if the firm proved or disproved the firm's hypothesis regarding the possible factors that may impact the size of the single unknown impurity. Mr. Dong stated no. I asked Mr. Dong if the firm performed any additional cleaning in response to this investigation. Mr. Dong stated no.

(PRINSTON00162382-162386 (emphasis added) (Ex. 20)). Thus, the FDA heavily criticized ZHP's conduct in this exact instance with regard to valsartan.

Moreover, this was a long-standing, ongoing cGMP problem with ZHP. [redacted] (Hai Wang 3/11/21 Dep. Tr., 559:4-8, 559:12-560:16 (Ex. 38)). Then, "When an out of specification result is obtained, current practice is [to] conduct a primary investigation, if no assignable cause is found, a process is filed and it's discussed there…The above practice reveals

major misinterpretation to the FDA guideline of the out of specification testing…" (*Id.* at 562:9-14, 562:17, 562:19-563:4). This is exactly what happened in August 2017, and is what the FDA pointed to in the EIR. This systemic problem that ZHP failed to rectify is not mentioned by ZHP in its motion, which is framed as if the deviation investigation deficiencies were an isolated, onetime event (as if that would be exculpatory, which it would not be anyway). ZHP's vague threat that if this is raised, there will be a mini-trial on this action is of no moment. There is no explanation for why that would be problematic. ZHP's failure to adequately evaluate OOS findings, as part of its overall failure to adequately evaluate the quality of the products it was manufacturing, and ill-conceived decision to destroy the entire batch without first complying with ZHP's own SOP requiring identification of the impurity and root cause, is relevant and presents no issues under F.R.E. 403.

3. ZHP's motion regarding the Charles Wang/Jim McDonald emails.

ZHP's motion is premised on a disingenuous presentation of the issue and the testimony from Min Li as to what occurred. On that basis, ZHP argues that Charles Wang was not acting as ZHP's agent—even though he was hired and paid by ZHP to advise it on the toxicity of NDMA and to draft ZHP's position on the issue. ZHP also ignores the fact that the testimony by Min Li documents ZHP's understanding of the risk level with NDMA, and the information available to the company in making its decisions on how to approach the upcoming meeting with the FDA—in

which ZHP hoped to convince the FDA to let ZHP continue to sell its contaminated API. Even if hearsay, which it is not, it would be admissible under the business records, state of mind, and notice exceptions to the hearsay rules, since it shows the information that was available to ZHP in charting its path forward.

The full facts are straightforward. On June 5/6, 2018, Min Li contacted Charles Wang, who was a toxicologist and the Director of the Safety Assessment group at another pharmaceutical company, GlaxoSmithKline. (Min Li 4/22/21 Dep. Tr. 538:20-539:10, 539:13-23, 540:1-3, 575:15-576:11 (Ex. 22)).

Min Li knew Charles Wang and trusted him as a reliable expert in toxicology, and contacted him "because we received a notice and we, you know, need to have an expertise, you know, to evaluate from the, you know, toxicological perspective." Further, "we didn't know anybody, you know, else in terms of the, you know, professional toxicologist, right? And due to the urgency, you know, you know, of this nature, we had to, you know, invoke him, right?" (*Id.* at 551:15-18, 551:21-552:6, 552:8-16, 577:7-10, 577:13-578:5).

Min Li sent Charles Wang a WHO article regarding the toxicology of NDMA. (*Id.* at 538:20-539:10, 540:1-9; *see also* ZHP02170975 (Ex. 39)). That article was then cited and quoted in Charles Wang's report, and the ZHP Deviation Investigation Report. (ZHP01881234 (Ex. 40); ZHP00004388 (Ex. 41)).

On June 10, 2018, Charles Wang sent Min Li a draft report as to the risk level

posed by NDMA, including a proposed limit of 0.011 ppm, but qualifying that suggestion with the caveat that, "**I can take out the limit of 0.011 parts per million if you are unable to achieve it**." (Min Li 4/22/21 Dep. Tr. 555:1-15 (quoting CHARLESWANGO00290 (Ex. 42)); *see also* ZHP02170920 (stating, [redacted]) (Ex. 43); PRINSTON00399001 (sending Charles Wang arguments from customers to refute) (Ex. 44)).

During his back and forth with Min Li, on June 22, 2018, Charles Wang advised that it would be helpful for him to also bring in another toxicologist with more specialized background as to carcinogens like NDMA: "I suggest Huahai to hire a carcinogenicity consultant to perform the analysis, who knows risk assessment of carcinogen and kept updated in regulatory guideline and standards in this field. If needed, I can recommend a couple to you for consideration." (Min Li 4/22/21 Dep. Tr. 573:7-574:5, 574:8-13).

Min Li agreed, and Charles Wang then reached out to Jim McDonald, a toxicologist with more specialized knowledge—for the purpose of advising ZHP at ZHP's request. Mr. Wang wrote on July 5, 2018 stating, "Friend of mine is looking forward a consultant in United States to help them define their product at FDA. Give me a call if you are interested…" He also advised Jim McDonald in a follow-up email, "My friend's company will have a face-to-face meeting with FDA to [decide,

sic] if they should recall their product in US market next Thursday and likes **to get some advice from people like you quickly**…their client in EU [Novartis] said [the limit] should be at 0.3 parts per million based on TD50 calculation…they would like to know if they can argue to set limit higher based on NDMA is considered a Class 2A carcinogen (limit at threshold of toxicological concern of 1.5 micrograms per day) and the longest duration of human exposure in US will be less than 3 years…Let me know if your company can help. I will ask them to contact you directly and send you more details." (*Id.* at 574:22-575:4, 575:7-13, 624:18-625:4, 628:22-629:4, 630:5-13, 631:14-22).

In this connection, Min Li confirmed, when asked, "**[A]t that point you were aware and you had authorized Mr. Wang to find an independent consultant for you?" that, "It looks like, yeah, we asked him probably, you know, yeah, to go ahead and try to find**." (*Id.* at 622:15-20, 622:23-623:1). Min Li also agreed that "as you said earlier, you had a lot of trust in Mr. Wang, considered him to be a reliable expert, so you asked him to go find you the most qualified person he could find basically." (*Id.* at 625:20-626:2).

Jim MacDonald,[2] who was told the contamination only reached 30 ppm, when it was actually at much higher levels, advised Charles Wang as to what he should tell ZHP: "NDMA (or dimethylnitrosamine) is a pretty well-known toxin and animal

[2] Plaintiffs have served James MacDonald with a trial subpoena.

carcinogen…the body of evidence on this suggests pretty clearly that this is a likely human carcinogen at sufficient exposures…The argument that the company would have to make to keep this product on the market will be very difficult with this profile. I'm not exactly sure where one would begin given the very high levels you think they are seeing….I think the strategy I would probably recommend would be to come up with a CMC plan to remove the contaminant (at least to minimally detectable levels) while they recall the existing product and reformulate. I expect this is not what they would want to hear but, unless there is a compelling reason to leave this product on the market (e.g.: only product available to treat a serious, life-threatening disease), I would expect the FDA would ask for a recall…this is not a good position for this product in my view." (*Id.* at632:4-633:1, 633:3-20, 638:24-639:19).

This information was shared with Min Li. When asked to confirm that, "Mr. Wang relayed to you that he had spoken with Jim MacDonald and what the result of that interaction had been after he had heard from Mr. MacDonald," Min Li confirmed, "I don't remember the details. **He probably talked to me verbally, at least.**" (*Id.* at 639:20-24, 640:3-4). He also confirmed that this information was provided to Jun Du, "**at a certain point, you know, he came to know**." (*Id.* at 650:14-18, 650:21-24). Charles Wang told Jim MacDonald, [redacted]. (CHARLESWANG000444 (emphasis

added) (Ex. 42)).

ZHP then followed Jim MacDonald's advice, quickly moving to develop an "optimized" version of the zinc chloride process that would quench the sodium azide with sodium nitrite but only when the "product" was separated out so it would not become contaminated. (Ex. 45). The patent, which was filed on July 17, 2018, even adopts his conclusion that NDMA is a "highly toxic impurity" and describes the new process as "ensuring the valsartan medication safety." (*Id.*).

Min Li and Jun Du confirmed that Charles Wang was paid for this work. (Jun Du 5/28/2021 Dep. Tr. 278:15-279:7 (Ex. 45); ZHP00675949 (Ex. 46)).

These facts clearly meet the standard set forth in the cases cited by ZHP. The first case—*Sanofi v. Lupin Atl. Holdings S.A.*, 282 F. Supp. 3d 818, 840 (D. Del. 2017)—concerned statements from doctors running an independent clinical study of a drug and held that those statements were hearsay. Here, Charles Wang was hired by ZHP, and was focused on giving ZHP what it was looking for—even offering to change his findings to raise the recommended levels allow ZHP to comply with them. (Min Li 4/22/21 Dep. Tr. 555:1-15 (quoting CHARLESWANGO00290 (Ex. Ex. 21))). He then consulted with James MacDonald after clearing that with ZHP, for ZHP's purposes, and adopted James MacDonald's objective advice as his own, although he was obviously willing to change that advice at ZHP's direction. (CHARLESWANG000444 (emphasis added) (Ex. 42); ZHP02170920 (Ex. 43);

PRINSTON00399001 (Ex. 44); ZHP01881288 (stating [redacted] (emphasis added)) (Ex. 50)).[3] The *Sanofi* court also failed to address whether the hearsay was admissible for any other purposes besides the truth of the matter asserted. As explained above, the emails are admissible under the state of mind and notice exceptions to the hearsay rules. Plaintiffs have subpoenaed Mr. MacDonald to confirm his advice and communications with Charles Wang in Court, invalidating any hearsay concerns.

The second case—*Mitchell v. Sun Drilling Prods., Inc.*, No. 95-1487, 1996

[3] Other courts have rejected arguments like ZHP's: "In the instant case, a large part of the evidence consists of emails by StreamCast CEO Michael Weiss, chairman Steven Griffin, chief technology officer Darrell Smith, director Bill Kallman, vice president for marketing Trey Bowles, network operations manager Derek Anderson, and software engineer Paul Panetti. StreamCast admits that these individuals served as its corporate officers or employees during the relevant time period. Another StreamCast employee, Jody Pace, was identified by Griffin's deposition testimony. Thus, emails sent by these individuals are all admissible non-hearsay under Rule 801(d)(2)(D). To the extent other content is incorporated into these emails, and to the extent the StreamCast agent expresses approval thereof, the incorporated content is admissible as vicarious adoptions. See [F.R.E.] 801(d)(2)(B). The record also contains a number of emails from Margaux Schaffer, a graphic design professional. StreamCast admits that Schaffer performed work for StreamCast during the relevant period, but argues that Schaffer's emails do not fall within the ambit of Rule 801(d)(2)(D) because she was an independent contractor rather than an employee. However, a statement is admissible under Rule 801(d)(2)(D) so long as it is made by an agent within the scope of agency, regardless of the precise contractual relationship between the agent and the party against whom the evidence is offered. [F.R.E.] 801(d)(2)(D)." *Metro-Goldwyn-Mayer v. Grokster*, 454 F. Supp. 2d 966, 973–74 (C.D. Cal. 2006).

WL 411613, at *2 (E.D. La. July 22, 1996)—concerned statements of non-employees without any discussion of agency and disregarded the exceptions to hearsay without any analysis. It does not help Defendants here. *Lippay v. Christos*, 996 F.2d 1490, 1498 (3d Cir. 1993), explained that "an agency relationship is established only where the party-opponent personally 'directed [the declarant's] work on a continuing basis.'" Here, Charles Wang requested ZHP approval to contact James MacDonald. ZHP provided that approval. Charles Wang then contacted James MacDonald, with ZHP's blessing, and adopted his advice as his own. Thus, throughout the relevant time period, ZHP was in control of Charles Wang's efforts, making him its agent. Additionally, Plaintiffs can call James MacDonald to confirm the contents of his emails. ZHP's remaining cases are equally distinguishable because ZHP did not hire Charles Wang for his independent advice.

As stated above, ZHP also ignores the fact that Min Li testified to the entire interaction, and his knowledge of the findings and advice, and this was passed on internally to Jun Du as well. Thus, this information was clearly obtained and communicated within the company for ZHP's purposes, is admissible, and the testimony about it constitutes an admission as to what ZHP did and why.

CONCLUSION

For the foregoing reasons, the Court should deny the ZHP Defendants' motions in limine.

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Respectfully submitted,

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